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     (FILE 'HOME' ENTERED AT 17:20:52 ON 04 JUN 2004)

     FILE 'CAPLUS' ENTERED AT 17:21:15 ON 04 JUN 2004
L1          1055 S 3(W)ADRENERG?
L2           261 S BETA3(L)ADRENERG?
L3            67 S L2(L)OBESITY
L4             4 S L3 AND PYRIDIN?
L5             0 S L2(L)PREMATURE
L6             1 S L2(L)LABOR
L7             0 S L2(L)DYSMENORRHEA
L8             0 S L2(L)PSYCHOS?
L9             0 S L2(L)PSYCHOSIS
L10            1 S L2(L)DEPRESSION
L11            2 S L2(L)GLAUCOMA
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L12 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:788390 CAPLUS
DN 137:37504
TI Uterine contractility: vaginal administration of the β-adrenergic agonist, terbutaline: Evidence of direct vagina-to-uterus transport
AU Bulletti, Carlo; De Ziegler, Dominique; De Moustier, Beatrice; Polli, Valeria; Bolelli, Gianfranco; Franceschetti, Franca; Flamigni, C.
CS 1st Institute of Obstetrics and Gynecology, University of Bologna, Bologna, 40138, Italy
SO Annals of the New York Academy of Sciences (2001), 943(Human Fertility and Reproduction), 163-171
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal
LA English
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Spontaneous uterine contractility during the menstrual cycle is required for menstruation, gamete transport, and, most likely, embryo nidation. Abnormal uterine contractility has been linked to **dysmenorrhea**, a condition associated with painful uterine cramping. Based on previous studies with progesterone, we have postulated the existence of a portal system that is responsible for some degree of direct vagina-to-uterus transport of administered compds. (i.e., the "first uterine pass effect"). It is possible that treatment with uterorelaxing substances, particularly β- **adrenergic** agonists, may alleviate the uterine discomfort that accompanies **dysmenorrhea**. However, side effects encountered with oral administration of β-agonists limit their utility. Alternatively, vaginal delivery of β-agonists could solve this dilemma by enhancing their efficacy and reducing side effects. Therefore, in the current study we used hysterectomy specimens and an in vitro uterine perfusion system to test the vagina-to-uterus transport of [3H]terbutaline, a well-known β-agonist. With the use of autoradiog. and scintillation counting techniques, our results clearly show progressive diffusion of labeled terbutaline from the rim of vaginal tissue through the uterus during the first 12 h of perfusion. This indicates that uterine targeting of terbutaline can be accomplished through vaginal administration, suggesting a new therapeutic modality in women's health care.

L12 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:215567 CAPLUS
DN 130:227768
TI A pharmaceutical composition comprising a β- **adrenergic** agonist in a bioadhesive carrier for treating **dysmenorrhea** and premature labor
IN Levine, Howard L.; Bologna, William J.; De Ziegler, Dominique
PA Columbia Laboratories, Inc., USA
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9913862	A2	19990325	WO 1998-US18538	19980908
	WO 9913862	A3	19990514		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6126959	A	20001003	US 1998-145172	19980901	
CA 2303339	AA	19990325	CA 1998-2303339	19980908	
AU 9891311	A1	19990405	AU 1998-91311	19980908	
AU 738460	B2	20010920			
EP 1011632	A2	20000628	EP 1998-943548	19980908	
EP 1011632	B1	20031112			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, LV, FI, RO

BR 9812134	A	20000718	BR 1998-12134	19980908	
NZ 502926	A	20011026	NZ 1998-502926	19980908	
JP 2002503637	T2	20020205	JP 2000-511486	19980908	
EP 1356806	A1	20031029	EP 2003-11701	19980908	

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, LT, LV, FI, RO, CY

AT 253892	E	20031115	AT 1998-943548	19980908	
RU 2219905	C2	20031227	RU 2000-108551	19980908	
ZA 9808328	A	19990223	ZA 1998-8328	19980911	
US 2002012677	A1	20020131	US 2000-510527	20000222	
US 6699494	B2	20040302			
NO 2000001287	A	20000310	NO 2000-1287	20000310	
MX 200002448	A	20001030	MX 2000-2448	20000310	
PRAI US 1997-58789P	P	19970912			
US 1998-145172	A	19980901			
EP 1998-943548	A3	19980908			
WO 1998-US18538	W	19980908			

TI A pharmaceutical composition comprising a β- **adrenergic** agonist in a bioadhesive carrier for treating **dysmenorrhea** and premature labor

AB A composition comprising a β- **adrenergic** agonist in a bioadhesive carrier is claimed for treating **dysmenorrhea** and premature labor. Preferably, the composition comprises terbutaline (I) in polycarbophil. Using this composition and the method of treatment provides sufficient local levels of the drug to provide therapeutic efficacy, but avoids many untoward adverse events. A topical composition containing 0.1% I and 20.0% polycarbophil was prepared Following a single dose regimen of the composition in female volunteers the Cmax = 117 pg/mL, Tmax = 13 h, T1/2 = 18 h and AUC 0to48 = 2281 pg.h/mL.

ST pharmaceutical beta **adrenergic** agonist bioadhesive **dysmenorrhea**; premature labor pharmaceutical beta **adrenergic** agonist

IT Adhesives
(biol.; pharmaceutical composition comprising β- **adrenergic** agonist in bioadhesive carrier for treating **dysmenorrhea** and premature labor)

IT Carboxylic acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxy, polymers, crosslinked; pharmaceutical composition comprising β- **adrenergic** agonist in bioadhesive carrier for treating **dysmenorrhea** and premature labor)

IT **Dysmenorrhea**
(pharmaceutical composition comprising β- **adrenergic** agonist in bioadhesive carrier for treating **dysmenorrhea** and premature labor)

IT Parturition
(premature; pharmaceutical composition comprising β- **adrenergic** agonist in bioadhesive carrier for treating **dysmenorrhea** and premature labor)

IT Drug delivery systems
(vaginal; pharmaceutical composition comprising β- **adrenergic** agonist in bioadhesive carrier for treating **dysmenorrhea** and

premature labor)

IT Adrenoceptor agonists
(β-; pharmaceutical composition comprising β- **adrenergic** agonist in bioadhesive carrier for treating **dysmenorrhea** and premature labor)

IT 9003-97-8, Polycarbophil. 23031-32-5, Terbutaline sulfate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition comprising β- **adrenergic** agonist in bioadhesive carrier for treating **dysmenorrhea** and premature labor)

L12 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:155621 CAPLUS
DN 124:194336
TI Use of β- **adrenergic** agonists for treatment of **dysmenorrhea**
IN Boyer, Christophe; Galichon, Bertrand
PA Fr.
SO Fr. Demande, 11 pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2720276	A1	19951201	FR 1994-6263	19940524
	FR 2720276	B1	19970905		
	WO 9719680	A1	19970605	WO 1995-FR1566	19951128
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 805679	A1	19971112	EP 1995-941150	19951128
	R: BE, CH, DE, ES, GB, IT, LI, NL, SE				
PRAI	FR 1994-6263		19940524		
	WO 1995-FR1566		19951128		

TI Use of β- **adrenergic** agonists for treatment of **dysmenorrhea**
AB β- **Adrenergic** agonists are used in pharmaceuticals for the treatment of **dysmenorrhea**. β- **Adrenergic** agonists can also be used with bradycardic agents, antiarrythmics, and inflammation inhibitors. Efficacy of salbutamol spray in treatment of patients with **dysmenorrhea** is reported.
ST **dysmenorrhea** treatment beta **adrenergic** agonist; salbutamol spray **dysmenorrhea** treatment
IT Antiarrhythmics
Dysmenorrhea
Inflammation inhibitors
(β- **adrenergic** agonists for treatment of **dysmenorrhea**)
IT Antiarrhythmics
(bradycardiacs, β- **adrenergic** agonists for treatment of **dysmenorrhea**)
IT Pharmaceutical dosage forms
(nasal, β- **adrenergic** agonists for treatment of **dysmenorrhea**)
IT **Adrenergic** agonists
(β-, β- **adrenergic** agonists for treatment of **dysmenorrhea**)
IT 13392-18-2, Fenoterol 18559-94-9, Salbutamol 18866-78-9, Colterol 23031-25-6, Terbutaline 26652-09-5, Ritodrine 30392-40-6, Bitolterol 38677-81-5, Pirbuterol 41570-61-0, Tulobuterol 56341-08-3, Mabuterol 89365-50-4, Salmeterol 130641-36-0, GR 63411
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(β- **adrenergic** agonists for treatment of **dysmenorrhea**)

L12 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1982:738 CAPLUS
DN 96:738
TI Pharmacological properties of a new peripheral analgesic, Suprofen
AU Rosenthale, M. E.; McGuire, J. L.; Capetola, R. J.
CS Res. Lab., Ortho Pharm. Corp., Raritan, NJ, 08869, USA
SO European Journal of Rheumatology and Inflammation (1981), 4(4), 469-80
CODEN: EJRIDH; ISSN: 0140-1610
DT Journal
LA English
AB Suprofen [40828-46-4] Is a new, non-narcotic analgesic agent. Using a spectrum of pharmacol. assays, including a new model of pathol. pain, Suprofen was shown to be a potent, orally effective peripheral analgesic having antiinflammatory and antipyretic properties. Using an in situ model for studying some factors related to **dysmenorrhea**, Suprofen was shown to inhibit arachidonic acid and prostaglandin (PG) induced uterine contractions, with the effectiveness or maximal response for Suprofen being significantly greater than that of other PG synthetase inhibitors tested such as indomethacin, naproxen, ibuprofen and aspirin. In vivo expts. describing analgesic and antiinflammatory activity, gastrointestinal safety ratios, effects on renal blood flow, uterine contractility, and **adrenergic** activation, all suggest that Suprofen possesses some tissue selectivity with respect to PG biosynthesis. Analgesic combination studies indicated that Suprofen potentiated the activity of paracetamol and narcotic analgesics such as codeine and butorphanol. Clin. studies with Suprofen have demonstrated efficacy in various painful conditions, including general and orthopedic surgery, periodontal surgery, third molar extraction, episiotomy, post partum pain, **dysmenorrhea**, and musculoskeletal disorders. Suprofen's analgesic profile is characterized by a rapid onset of action with a duration of 4-6 h. Comparative efficacy studies have demonstrated that 200 mg of Suprofen provides pain relief at least equivalent to the combination of 650 mg aspirin and 60 mg codeine.

L12 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1963:471232 CAPLUS
DN 59:71232
OREF 59:13234c
TI Pharmacology
AU Woodbury, Robert A.
CS Univ. of Tennessee, Memphis
SO New Basic Concepts Pharm. Sci., Ann. Visiting, Lecture Ser. (1962), 5, 88-92
DT Journal
LA Unavailable
AB Mechanisms whereby drugs modify the actions of other drugs, influence of drugs on **adrenergic** receptors of blood vessels, and mechanisms of action of drugs affording relief to patients with **dysmenorrhea** are outlined.

F 2 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:1006955 CAPLUS
DN 140:42044
TI Preparation of cyclic amines as β3-adrenergic receptor agonists and medicinal composition containing the same
IN Ueno, Yoshihide; Sawada, Nobuyuki; Umezome, Takashi
PA Sumitomo Pharmaceuticals Co., Ltd., Japan
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003106423	A1	20031224	WO 2003-JP7383	20030610

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI JP 2002-171411 A 20020612
OS MARPAT 140:42044
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Cyclic amine compds. such as 1,2,3,4-tetrahydroquinoline and 1,2,3,4,5-tetrahydro-1H-1-benzazepine derivs. represented by the formula (I) [wherein R1 = (un)substituted lower alkyl, X1-R1a-CONR1aR1b, X1-R1e-CO2R1a, X1-R1d; wherein X1 = a single bond, O, S, NR1c, NR1cSO2, SO2NR1c, CONR1cSO2; R1e = a single bond, (un)substituted lower alkylene; R1a, R1b, R1c = H, (un)substituted lower alkyl; or NR1aR1b = an (un)substituted 3- to 8-membered saturated cyclic amino optionally containing O or NH in the ring; R2 = H, halo, each (un)substituted lower alkyl, alkenyl, or NH2, OH, lower alkoxy; or R1 and R2 together forms methylenedioxy; R4, R5 = H, (un)substituted alkyl; one of X and Y = CH2 and the other = (un)substituted NH; n = an integer of 1-3; Ar = (un)substituted Ph or pyridyl, Q; wherein Z1 = O, S; R11 = H, lower alkyl, SO2R14, (un)substituted H2; R12 = O, S, H2; R13 = O, H2] or pharmaceutically acceptable salts of the compds. The compds. I or salts thereof have a stimulating activity on a β3- **adrenergic** receptor. They are useful as therapeutic agents for obesity, hyperglycemia, increased urinary frequency (pollakiuria), **depression**, and gallstone. Thus, alkylation of N-[(2R)-2-(3-chlorophenyl)-2-hydroxyethyl]-N-(7-hydroxy-1-tosyl-2,3,4,5-tetrahydro-1H-benzazepin-4-yl)carbamic acid tert-Bu ester by Et bromoacetate in the presence of K2CO3 in acetone at room temperature for 19 h gave 72% [[4-[4-(tert-butoxycarbonyl)-N-[(2R)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]-1-tosyl-2,3,4,5-tetrahydro-1H-1-benzazepin-4-yl]oxy]acetic acid which was treated with CF3CO2H in CH2Cl2 at room temperature for 4 h and the with MeSO3H and thioanisole in CF3CO2H while warming from ice-temperature to room temperature for 15 h with stirring to give 85% [[4-[[(2R)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]-2,3,4,5-tetrahydro-1H-1-benzazepin-4-yl]oxy]acetic acid Et ester (II). II at 10 mg/kg p.o. increased the serum free fatty acid by 0.42 mEa/L in ICR mice.

ST cyclic amine prepn **beta3 adrenergic** receptor agonist; tetrahydroquinoline tetrahydrobenzazepine prepn treatment obesity; hyperglycemia pollakiuria gallstone treatment cyclic amine prepn; increased urinary frequency **depression** gallstone treatment

cyclic amine prepn; tetrahydrobenzazepinyloxyacetic acid ethyl ester prepn
treatment hyperglycemia

IT Amines, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic; preparation of cyclic amines as β3- **adrenergic** receptor agonists for treatment of obesity, hyperglycemia, increased urinary frequency (pollakiuria), **depression**, and gallstone)

IT Mental disorder
(**depression**; preparation of cyclic amines as β3- **adrenergic** receptor agonists for treatment of obesity, hyperglycemia, increased urinary frequency (pollakiuria), **depression**, and gallstone)

IT Antidepressants
Antidiabetic agents
Antiobesity agents
Calculi, biliary
Hyperglycemia
Obesity
(preparation of cyclic amines as β3- **adrenergic** receptor agonists for treatment of obesity, hyperglycemia, increased urinary frequency (pollakiuria), **depression**, and gallstone)

IT Urinary tract, disease
(urinary frequency; preparation of cyclic amines as β3- **adrenergic** receptor agonists for treatment of obesity, hyperglycemia, increased urinary frequency (pollakiuria), **depression**, and gallstone)